

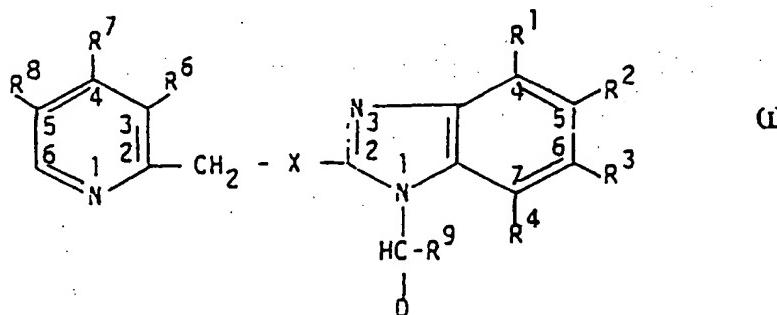
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(54) Title: NEW BENZIMIDAZOLE DERIVATIVES A PROCESS FOR PRODUCTION THEREOF AND A PHARMACEUTICAL COMPOSITION CONTAINING THE SAME



(57) Abstract

Novel compounds of formula (I), pharmaceutical compositions containing such compounds as active ingredient, and the use of the compounds in medicine.

Examples I 21 and I 22

1-chloromethyl-(5-methoxy) and (6-methoxy)-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole.

1-hydroxy methyl-(5-methoxy) and -(6-methoxy)-2-[[-(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (30 g 0.08 mol ratio 1:2) was dissolved in toluene (500 ml) and the solution was cooled to -30°C. A solution of thionyl chloride (19 g 0.16 mol) in toluene (100 ml) was added dropwise at -30°C and the mixture was stirred for 10 minutes at -30°C. Then a solution of triethyl amine (45 g 0.45 mol) in toluene (200 ml) was added dropwise. After the addition the temperature was raised and the mixture stirred at room temperature for 30 minutes. The mixture was evaporated and the residue (120 g) was chromatographed on silica gel (ethylacetate-methylenechloride 50-50) giving the title compound as an isomeric mixture (ratio 1:3) Yield 11.9 g.

NMR (500 MHz, CDCl₃) 2.23, 2.25, 2.26, 3.72, 3.87, 3.92, 4.88, 4.95, 4.96, 6.17, 6.18, 6.54, 6.57, 6.95, 7.01, 7.19, 7.26, 7.43, 7.67, 8.17. If desired the pure 1-chloromethyl 6-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole was obtained when the isomeric mixture was crystallized in acetonitrile. NMR (500 MHz, CDCl₃) 2.23, 2.25, 3.72, 3.92, 4.88, 4.96, 6.17, 6.57, 6.95, 7.01, 7.67, 8.17.

Preparation of Phosphoric acid, cyanoethyl-1-[6-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole-1-yl]methyl diester, triethylammonium salt (Method B)

1-Chloromethyl-6-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (0.90 g, 0.0023 mol) was added under stirring to a solution of mono-triethylammonium salt of phosphoric acid cyanoethyl ester (0.70 g, 0.0028 mol) and triethyl amine (0.65 g, 0.0064 mol)